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EXAMINER	
PANARO, NICHOLAS J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 03/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

AL

Office Action Summary	Application No.	Applicant(s)	
	09/574,386	ALBERTSON ET AL.	
	Examiner	Art Unit	
	Nicholas J. Panaro	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-19,23 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-19,23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/30/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-9, 11-15 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 7, it is vague and indefinite what is meant by the phrase "at least about 50 kilobases". The phrase "at least" typically indicates a minimum point. The phrase "at least" however, is contraverted by the term "about" which implies that values above and below 50 kilobases are permitted. Further, the extent of variance permitted by "about" is unclear in this context. Since nucleotides are whole numbers, "about 50 kilobases" cannot mean from 49,000.5 to 51,000.5 bases because nucleotides cannot be split in half. Therefore, it is also unclear if "about 50 kilobases" simply includes 49 kilobases or if it also includes 1-48 kilobases as well. In Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (CAFC 1991), the CAFC stated, "The district court held claims 4 and 6 of the patent invalid because their specific activity limitation of "at least about 160,000" was indefinite". After review, the CAFC states "We therefore affirm the district court's determination on this issue." Thus, the CAFC found the phrase "at least about" indefinite where the metes and bounds of the term were not defined in the specification.

Regarding claim 8, it is vague and indefinite what is meant by the phrase "at least about 100 kilobases". The phrase "at least" typically indicates a minimum point. The phrase "at least" however, is contraverted by the term "about" which implies that values above and below 100 kilobases are permitted. Further, the extent of variance permitted by "about" is unclear in this context. Since nucleotides are whole numbers, "about 100 kilobases" cannot mean from 99,000.5 to 100,000.5 bases because

nucleotides cannot be split in half. Therefore, it is also unclear if "about 100 kilobases" simply includes 99 kilobases or if it also includes 1-98 kilobases as well. In Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (CAFC 1991), the CAFC stated, "The district court held claims 4 and 6 of the patent invalid because their specific activity limitation of "at least about 160,000" was indefinite". After review, the CAFC states "We therefore affirm the district court's determination on this issue." Thus, the CAFC found the phrase "at least about" indefinite where the metes and bounds of the term were not defined in the specification.

Regarding claim 9, it is vague and indefinite what is meant by the phrase "of less than about 500 kilobases". The phrase "of less than" typically indicates a maximum point. The phrase "of less than" however, is contraverted by the term "about" which implies that values above and below 500 kilobases are permitted. Further, the extent of variance permitted by "about" is unclear in this context. Since bases (i.e., nucleotides) are whole numbers, "about 500 kilobases" cannot mean from 490,000.5 to 510,000.5 bases because bases cannot be split in half. Therefore, it is also unclear if "about 500 kilobases" simply includes 499 kilobases or if it also includes 1-498 kilobases as well. Thus, the phrase "of less than about" is indefinite wherein the metes and bounds of the term were not defined in the specification.

Regarding claim 11, it is vague and indefinite what is meant by the phrase "less than about 5 kilobases". The phrase "less than" typically indicates a maximum point. The phrase "less than" however, is contraverted by the term "about" which implies that values above and below 5 kilobases are permitted. Further, the extent of variance permitted by "about" is unclear in this context. Since bases (i.e., nucleotides) are whole numbers, "about 5 kilobases" cannot mean from 49,000.5 to 51,000.5 bases because bases cannot be split in half. Therefore, it is also unclear if "about 5 kilobases" simply includes 4 kilobases or if it also includes 1-3 kilobases as well. Thus, the phrase "at least about" is indefinite wherein the metes and bounds of the term were not defined in the specification.

Regarding claim 12, it is vague and indefinite what is meant by the phrase "less than about 2

kilobases". The phrase "less than" typically indicates a maximum point. The phrase "less than" however, is contraverted by the term "about" which implies that values above and below 2 kilobases are permitted. Further, the extent of variance permitted by "about" is unclear in this context. Since bases (i.e., nucleotides) are whole numbers, "about 2 kilobases" cannot mean from 1900.5 to 2100.5 bases because bases cannot be split in half. Therefore, it is also unclear if "about 2 kilobases" simply includes 4 kilobases or if it also includes 1-3 kilobases as well. Thus, the phrase "less than about" is indefinite wherein the metes and bounds of the term were not defined in the specification.

Regarding claim 13, it is vague and indefinite what is meant by the phrase "greater than about 100 basepairs". The phrase "greater than about" typically indicates a minimum point. The phrase "greater than about" however, is contraverted by the term "about" which implies that values above and below 100 basepairs are permitted. Further, the extent of variance permitted by "about" is unclear in this context. Since bases are whole numbers, "about 100 basepairs" cannot mean from 98.5 to 101.5 basepairs because bases cannot be split in half. Therefore, it is also unclear if "about 100 basepairs" simply includes 99 basepairs or if it also includes 1-98 basepairs as well. Thus, the phrase "greater than about" is indefinite wherein the metes and bounds of the term were not defined in the specification.

Regarding claim 14, it is vague and indefinite what is meant by the phrase "less than about 2 nanoliters". The phrase "less than" typically indicates a maximum point. The phrase "less than" however, is contraverted by the term "about" which implies that values above and below 2 nanoliters are permitted. Further, the extent of variance permitted by "about" is unclear in this context. Therefore, it is also unclear if "about 2 nanoliters" simply includes 1.9 nanoliters or if it also includes 0 to 1.8 nanoliters as well. Thus, the phrase "less than about" is indefinite wherein the metes and bounds of the term were not defined in the specification.

Regarding claim 15, it is vague and indefinite what is meant by the phrase "greater than about 0.002 nanoliters". The phrase "greater than" typically indicates a minimum point. The phrase "greater

than" however, is contraverted by the term "about" which implies that values above and below 0.002 nanoliters are permitted. Further, the extent of variance permitted by "about" is unclear in this context. Therefore, it is also unclear if "about 0.002 nanoliters" simply includes 0.0019 nanoliters or if it also includes 0 to 0.0018 nanoliters as well. Thus, the phrase "greater than about" is indefinite wherein the metes and bounds of the term were not defined in the specification.

Regarding claim 25, it is vague and indefinite what is meant by the phrase "at least about 20 kilobases". The phrase "at least" typically indicates a minimum point. The phrase "at least" however, is contraverted by the term "about" which implies that values above and below 20 kilobases are permitted. Further, the extent of variance permitted by "about" is unclear in this context. Since nucleotides are whole numbers, "about 20 kilobases" cannot mean from 19,000.5 to 21,000.5 bases because nucleotides cannot be split in half. Therefore, it is also unclear if "about 20 kilobases" simply includes 19 kilobases or if it also includes 1-18 kilobases as well. In Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (CAFC 1991), the CAFC stated, "The district court held claims 4 and 6 of the patent invalid because their specific activity limitation of "at least about 160,000" was indefinite". After review, the CAFC states "We therefore affirm the district court's determination on this issue." Thus, the CAFC found the phrase "at least about" indefinite where the metes and bounds of the term were not defined in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application

> by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 3-13, 18 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Rabinovitch (U.S. Patent 5,814,444; issued September 29, 1998) as evidenced by Lisitsyn et al (Science 259: 946-951, 1993) and as further evidenced by Strachan and Read (Human Molecular Genetics 2, John Wiley & Sons, Inc., F. Kingston (ed.), pp. 82-93, 1999).

Regarding claim 1, Rabinovitch teaches a method for preparing an array of polynucleotides that is representative of a plurality of first polynucleotides comprising: (a) providing a plurality of samples of double stranded polynucleotide fragments, wherein each sample is derived from a first polynucleotide (Rabinovitch column 2, lines 32-35, 39-43; column 3 lines 31-37); (b) Rabinovitch teaches the PCR adapter-mediated amplification of Lisitsyn et al (Rabinovitch column 3, lines 37-41; column 14, lines 45-48; column 22, lines 4-7; Lisitsyn et al, figures 1 and 2). Because Rabinovitch teaches Lisitsyn et al, Rabinovitch teaches ligating adapters to each end of the polynucleotide fragments of each sample to produce modified polynucleotide fragments, wherein each adapter comprises a first strand and a second strand, the second strand having a region of substantial complementarity to a region of the first strand (Lisitsyn et al, figures 1 and 2); (c) Rabinovitch teaches the PCR adapter-mediated amplification of Lisitsyn et al (Rabinovitch column 3, lines 37-41; column 14, lines 45-48; column 22, lines 4-7; Lisitsyn et al, figures 1 and 2). Because Rabinovitch teaches Lisitsyn et al, Rabinovitch teaches using sequences within the adapters to amplify the modified polynucleotide fragments to produce an amplification product for each sample of polynucleotide fragments (Lisitsyn et al, figures 1 and 2), wherein each amplification product is representative of the first polynucleotide corresponding to each sample (each amplification

product can be interpreted as being "representative" of the first polynucleotide because said amplification products are copied via the polymerase chain reaction from a section of the first polynucleotide); and (d) applying target solutions comprising the amplification products to one or more substrates, wherein each target solution is applied to a distinct location on one substrate and/or target solutions are applied to different substrates that are combined, whereby target solution polynucleotides are immobilized on the substrate(s) to form the target elements of an array of polynucleotides (Rabinovitch column 8, line 63 – column 9, lines 6-10, 21-24, 34-38, 51-57; column 10, lines 1-9; column 20, line 45 – column 21, line 20).

Regarding claim 3, Rabinovitch teaches a method wherein the double-stranded polynucleotide fragments are derived from a polynucleotide library (i.e., chromosomal fragments, column 2, lines 39-43).

Regarding claim 4, Rabinovitch teaches a method wherein the polynucleotide library is a genomic DNA library (column 17, line 34 – column 18, line 2; column 20, line 45 – column 21, line 20).

Regarding claim 5, Rabinovitch teaches a method wherein the polynucleotide is a cDNA (Rabinovitch column 4, lines 44-53).

Regarding claim 6, Rabinovitch teaches a method wherein the double-stranded polynucleotide fragments are derived from YAC (column 1, lines 61-67).

Regarding claim 7, Rabinovitch teaches YACs (column 1, lines 61-67). Rabinovitch does not explicitly teach the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 50 kilobases. Strachan and Read teach polynucleotides having a complexity of at least about 50 kilobases, e.g., a YAC vector containing an insert of greater than 200 kb (Strachan and Read, pg. 87, Table 4.2). Therefore, by teaching the YACs, Rabinovitch inherently teaches the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 50 kilobases.

Regarding claim 8, Rabinovitch teaches YACs (column 1, lines 61-67). Rabinovitch does not explicitly teach the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 100 kilobases. Strachan and Read teach polynucleotides having a complexity of at least about 100 kilobases (e.g., a YAC vector containing an insert of greater than 200 kb, Strachan and Read, pg. 87, Table 4.2). Therefore, by teaching YACs, Rabinovitch inherently teaches the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 100 kilobases.

Regarding claim 9, Rabinovitch teaches YACs (column 1, lines 61-67). Rabinovitch does not explicitly teach the use of polynucleotides wherein the polynucleotides each have a complexity of less than about 500 kilobases. Strachan and Read teach polynucleotides having a complexity of less than about 500 kilobases (e.g., a YAC vector containing an insert of 200 kb, Strachan and Read, pg. 87, Table 4.2). Therefore, by teaching YACs, Rabinovitch inherently teaches the use of polynucleotides wherein the polynucleotides each have a complexity of less than about 500 kilobases.

Regarding claim 10, Rabinovitch teaches the double-stranded polynucleotide fragments are obtained using one or more restriction endonucleases (column 2, lines 32-34; column 14, lines 38-44).

Regarding claim 11, Rabinovitch teaches the average length of the double-stranded polynucleotide fragments is less than about 5 kilobases (i.e., 200-1000 basepairs, column 15, lines 26-28).

Regarding claim 12, Rabinovitch teaches the average length of the double-stranded polynucleotide fragments is less than about 2 kilobases (i.e., 200-1000 basepairs, column 15, lines 26-28).

Regarding claim 13, Rabinovitch teaches the average length of the double-stranded polynucleotide fragments is greater than about 100 basepairs (i.e., 200-1000 basepairs, column 15, lines 26-28).

Regarding claim 18, Rabinovitch teaches amplification of nucleic acids with adapters (column 14, lines 45-48). The adapter oligonucleotides R Bgl 24 and R Bgl 12 described by (Lisitsyn et al, pg. 949, Table 1) comprise adenosine, cytosine and guanine residues each of which possess amino groups. Therefore, Rabinovitch inherently teaches adapters with amino groups.

Regarding claim 25, Rabinovitch teaches YACs (column 1, lines 61-67). Rabinovitch does not explicitly teach the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 20 kilobases. Strachan and Read teach polynucleotides having a complexity of at least about 20 kilobases, e.g., a YAC vector containing an insert of greater than 200 kb (Strachan and Read, pg. 87, Table 4.2). Therefore, by teaching YACs, Rabinovitch inherently teaches the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 20 kilobases.

Claims 1, 3-13, 18 and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Gray et al (U.S. Patent 6,465,182; filed April 29, 1999; issued October 15, 2002) as evidenced by Klein et al (PNAS 96: 4494-4499, 1999) and as further evidenced by Strachan and Read (Human Molecular Genetics 2, John Wiley & Sons, Inc., F. Kingston (ed.), pp. 82-93, 1999).

The applied reference has a common assignee (The Regents of the University of California) and common inventors (Daniel Pinkel and Donna Albertson) with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Gray et al teach a method for preparing an array of polynucleotides that is representative of a plurality of first polynucleotides comprising: (a) providing a plurality of samples of double stranded polynucleotide fragments, wherein each sample is derived from a first polynucleotide (Gray et al column 6, lines 17-41); (b) Gray et al teach Klein et al (Gray et al, column 11, line 19). Klein et al teach ligating adapters to each end of the polynucleotide fragments of each sample to produce modified polynucleotide fragments, wherein each adapter comprises a first strand and a second strand, the second strand having a region of substantial complementarity to a region of the first strand (Klein et al, pp. 4494-4495 and Figure 1). Therefore, Gray et al teach ligating adapters to each end of the polynucleotide fragments of each sample to produce modified polynucleotide fragments, wherein each adapter comprises a first strand and a second strand, the second strand having a region of substantial complementarity to a region of the first strand; (c) using sequences within the adapters to amplify the modified polynucleotide fragments to produce an amplification product for each sample of polynucleotide fragments, wherein each amplification product is representative of the first polynucleotide corresponding to each sample (Gray et al column 10, lines 44-59; column 11, lines 1-20; column 14, lines 34-54); and (d) applying target solutions comprising the amplification products to one or more substrates, wherein each target solution is applied to a distinct location on one substrate and/or target solutions are applied to different substrates that are combined, whereby target solution polynucleotides are immobilized on the substrate(s) to form the target elements of an array of polynucleotides (Gray et al column 5, lines 18-21; column 6, lines 50-65; column 7, lines 30-67; column 8, lines 36-52).

Regarding claim 3, Gray et al teach a method wherein the double-stranded polynucleotide fragments are derived from a polynucleotide library (i.e., restriction fragments derived from chromosomes or genomic DNA, column 6, lines 17-26).

Regarding claim 4, Gray et al teach a method wherein the polynucleotide library is a genomic DNA library (column 6, lines 17-26).

Regarding claim 5, Gray et al teach a method wherein the polynucleotide is a cDNA (column 6, lines 17-26).

Regarding claim 7, Gray et al teach chromosome fragments (column 1, lines 47-67; column 6, lines 17-26; column 6, lines 50-63). Gray et al do not explicitly teach the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 50 kilobases. Strachan and Read teach polynucleotides having a complexity of at least about 50 kilobases, e.g., a human DNA restriction fragment of 78 kilobases (Strachan and Read, pg. 75, Table 4.1). Therefore, by teaching the chromosomes, Gray et al inherently teach the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 50 kilobases.

Regarding claim 8, Gray et al teach chromosome fragments (column 1, lines 47-67; column 6, lines 17-26; column 6, lines 50-63). Gray et al do not explicitly teach the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 100 kilobases. Strachan and Read teach polynucleotides having a complexity of at least about 100 kilobases, e.g., a human DNA restriction fragment of 390 kilobases (Strachan and Read, pg. 75, Table 4.1). Therefore, by teaching the chromosomes, Gray et al inherently teach the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 100 kilobases

Regarding claim 9, Gray et al teach chromosome fragments (column 1, lines 47-67; column 6, lines 17-26; column 6, lines 50-63). Gray et al do not explicitly teach the use of polynucleotides wherein the polynucleotides each have a complexity of less than about 500 kilobases. Strachan and Read teach polynucleotides having a complexity of less than about 500 kilobases, e.g., a human DNA restriction fragment of 390 kilobases (Strachan and Read, pg. 75, Table 4.1). Therefore, by teaching chromosomes, Gray et al inherently teaches the use of polynucleotides wherein the polynucleotides each have a complexity of less than about 500 kilobases.

Regarding claim 10, Gray et al teach the double-stranded polynucleotide fragments are obtained using one or more restriction endonucleases (column 6, lines 20-25).

Regarding claim 11, Gray et al teach Klein et al (Gray et al, column 11, line 19). Klein et al teach the average length of the double-stranded polynucleotide fragments is less than about 5 kilobases (i.e., 200-2000 basepairs, Klein et al pp. 4495-4496).

Regarding claim 12, Gray et al teach Klein et al (Gray et al, column 11, line 19). Klein et al teach the average length of the double-stranded polynucleotide fragments is less than about 2 kilobases (i.e., 200-2000 basepairs, Klein et al pp. 4495-4496).

Regarding claim 13, Gray et al teach Klein et al (Gray et al, column 11, line 19). Klein et al teach the average length of the double-stranded polynucleotide fragments is greater than about 100 basepairs (i.e., 200-2000 basepairs, Klein et al pp. 4495-4496).

Regarding claim 18, Gray et al teach Klein et al (Gray et al, column 11, line 19). Gray et al teach amplification of nucleic acids with adapters (column 11, lines 1-20; column 14, lines 34-67). The adapter oligonucleotides MseLig 21 and MseLig 12 described by (Klein et al, pg. 4494) comprise adenosine, cytosine and guanine residues each of which possess amino groups. Therefore, Gray et al inherently teach adapters with amino groups.

Regarding claim 25, Gray et al teach chromosome fragments (column 1, lines 47-67; column 6, lines 17-26; column 6, lines 50-63). Gray et al do not explicitly teach the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 20 kilobases. Strachan and Read teach polynucleotides having a complexity of at least about 20 kilobases, e.g., a human DNA restriction fragment of 78 kilobases (Strachan and Read, pg. 75, Table 4.1). Therefore, by teaching the

chromosomes, Gray et al inherently teach the use of polynucleotides wherein the polynucleotides each have a complexity of at least about 20 kilobases.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rabinovitch (U.S. Patent 5,814,444; issued September 29, 1998) in view of Schreiber et al (U.S. 6,824,987; filed May 10, 2000).

Rabinovitch teaches a method for preparing an array of polynucleotides for genomic DNA.

Regarding Claim 14, Rabinovitch does not teach the average volume of each target solution applied to the substrate is less than about 2 nanoliters. Schreiber et al teach a method of making an array to identify small molecule partners for biological macromolecules (e.g., polynucleotides, Schreiber et al column, line 61 – column line 46, esp. column 2, lines 31-40). Schreiber et al teach the average volume of each target solution applied to the substrate is less than about 2 nanoliters (1 nanoliter samples; column 6, line 56 – column 7, line 19) for the advantage of extreme miniaturization (column 6, lines 64-66). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add the method of Schreiber et al to the method of Rabinovitch for the advantage of extreme miniaturization (column 6, lines 64-66).

Regarding Claim 15, Rabinovitch does not teach the average volume of each target solution applied to the substrate equal to or greater than about 0.002 nanoliters. Schreiber et al teach a method

of making an array to identify small molecule partners for biological macromolecules (e.g., polynucleotides, Schreiber et al column, line 61 – column line 46, esp. column 2, lines 31-40). Schreiber et al teach the average volume of each target solution applied to the substrate equal to or greater than about 0.002 nanoliters (1 nanoliter samples; column 6, line 56 – column 7, line 19) for the advantage of extreme miniaturization (column 6, lines 64-66).

Claims 16-17 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rabinovitch (U.S. Patent 5,814,444; issued September 29, 1998) and Pollack et al (Nature Genetics Vol. 23, pp.41-46; published September 1999) as evidenced by DeRisi et al (Science Vol. 278, pp. 680-686; published October 24, 1997).

Rabinovitch teaches a method for preparing an array of polynucleotides from genomic DNA.

Regarding claim 16, Rabinovitch does not teach a microarray wherein the density of the array compounds comprises at least 1000 spots per cm^2. Pollack et al teach comparative genomic hybridization using cDNA arrays. As evidenced by DeRisi et al (DeRisi et al, pg. 686, last paragraph and Figure 1), the array of Pollack et al contained a DNA microarray containing 6400 spots on a 18 x 18 mm surface (i.e., approximately 1975 spots per square centimeter; DeRisi et al, pg. 686, last paragraph and Figure 1).

Regarding claim 17, Rabinovitch does not teach a microarray made by a robotic device. Pollack et al teach target solutions robotically spotted on a substrate as evidenced by DeRisi et al (DeRisi et al, pg. 686, last paragraph and Figure 1).

Regarding claim 23, Rabinovitch does not explicitly teach each amplification product for each sample is isolated and resuspended to form the target solution for that sample. Pollack et al teaches DeRisi et al (Pollack et al, pg. 45, last paragraph). DeRisi et al teaches the use of cDNA generated from mRNA via reverse transcription (DeRisi et al, pg. 680, paragraph 5) and the subsequence resuspension of said cDNA to fabricate a cDNA array (DeRisi et al, pg. 680, paragraph 5; DeRisi et al, pg.686, citations 11 and 12). Polack et al teach the use of PCR-amplified cDNAs in combination with the teachings of

DeRisi et al to fabricate a cDNA array wherein each amplification product for each sample is isolated and resuspended to form the target solution.

One of ordinary skill in the art would have been motivated to combine the teachings of Rabinovitch and Pollack et al for the advantage of identifying gene amplifications and deletions genome-wide and with high resolution and comparing alterations in DNA copy number and gene expression (Pollack et al, pg. 41, Abstract).

Claims 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al (U.S. Patent 6,465,182; filed April 29, 1999; issued October 15, 2002) in view of Schreiber et al (U.S. 6,824,987; filed May 10, 2000).

Gray et al a method for preparing an array of polynucleotides for genomic DNA.

Regarding Claim 14, Gray et al do not teach the average volume of each target solution applied to the substrate is less than about 2 nanoliters. Schreiber et al teach a method of making an array to identify small molecule partners for biological macromolecules (e.g., polynucleotides, Schreiber et al column, line 61 – column line 46, esp. column 2, lines 31-40). Schreiber et al teach the average volume of each target solution applied to the substrate is less than about 2 nanoliters (1 nanoliter samples; column 6, line 56 – column 7, line 19) for the advantage of extreme miniaturization (column 6, lines 64-66). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add the method of Schreiber et al to the method of Gray et al for the advantage of extreme miniaturization (column 6, lines 64-66).

Regarding Claim 15, Gray et al do not teach the average volume of each target solution applied to the substrate equal to or greater than about 0.002 nanoliters. Schreiber et al teach a method of making an array to identify small molecule partners for biological macromolecules (e.g., polynucleotides, Schreiber et al column, line 61 – column line 46, esp. column 2, lines 31-40). Schreiber et al teach the average volume of each target solution applied to the substrate equal to or greater than about 0.002

nanoliters (1 nanoliter samples; column 6, line 56 – column 7, line 19) for the advantage of extreme miniaturization (column 6, lines 64-66).

Claims 16-17 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al (U.S. Patent 6,465,182; filed April 29, 1999; issued October 15, 2002) and Pollack et al (Nature Genetics Vol. 23, pp.41-46; published September 1999) as evidenced by DeRisi et al (Science Vol. 278, pp. 680-686; published October 24, 1997).

Gray et al teach a method for preparing an array of polynucleotides for genomic DNA.

Regarding claim 16, Gray et al does not teach a microarray wherein the density of the array compounds comprises at least 1000 spots per cm^2 wherein said compound may be a polynucleotide. Pollack et al teach comparative genomic hybridization using cDNA arrays. As evidenced by DeRisi et al (DeRisi et al, pg. 686, last paragraph and Figure 1), the array of Pollack et al contained a DNA microarray containing 6400 spots on a 1.8 x 18 mm surface (i.e., approximately 1975 spots per square centimeter; DeRisi et al, pg. 686, last paragraph and Figure 1).

Regarding claim 17, Gray et al do not teach a microarray made by a robotic device. Pollack et al teach target solutions robotically spotted on a substrate as evidenced by DeRisi et al (DeRisi et al, pg. 686, last paragraph and Figure 1).

Regarding claim 23, Gray et al do not explicitly teach each amplification product for each sample is isolated and resuspended to form the target solution for that sample. Pollack et al teaches DeRisi et al (Pollack et al, pg. 45, last paragraph). DeRisi et al teaches the use of cDNA generated from mRNA via reverse transcription (DeRisi et al, pg. 680, paragraph 5) and the subsequence resuspension of said cDNA to fabricate a cDNA array (DeRisi et al, pg. 680, paragraph 5; DeRisi et al, pg.686, citations 11 and 12). Polack et al teach the use of PCR-amplified cDNAs in combination with the teachings of DeRisi et al to fabricate a cDNA array wherein each amplification product for each sample is isolated and resuspended to form the target solution.

One of ordinary skill in the art would have been motivated to combine the teachings of Gray et al and Pollack et al for the advantage of identifying gene amplifications and deletions genome-wide and with

high resolution and comparing alterations in DNA copy number and gene expression (Pollack et al, pg. 41, Abstract).

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gray et al (U.S. Patent 6,465,182; filed April 29, 1999; issued October 15, 2002).

Gray et al teach the target solution comprises dimethyl sulfoxide (column 9, lines 62-67). It would have been prima facie obvious to perform routine optimization using reagents, as noted in *In re Aller*, 105 USPQ 233 at 235. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection specific buffer concentrations was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

It would have been obvious to one of ordinary skill in the art to optimize the concentration of dimethyl sulfoxide in the solution by testing a wide range of concentrations including 20% dimethyl sulfoxide to obtain the best result.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicholas J. Panaro whose telephone number is (571) 272-0778. The examiner can normally be reached on Monday - Friday 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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2/25/2005